This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. CERTIFICATE NUMBER: 57-R-0003

CUSTOMER NUMBER: 896

FORM APPROVED
OMB NO. 0579-0036

Emory University
1599 Clifton Rd NE, 1599-001-1BE
Atlanta, GA 30322

Telephone: (404) 727-3889

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, or experimentation or held for these purposes. Attach additional sheets if necessary)

FACILITY LOCATIONS (Sites) – See Attached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY **(Attach additional sheets if necessary or use APHIS FORM 7023A)**

A. Animals Covered By The Animal Welfare Regulations	**B.** Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	**C.** Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	**D.** Number of animal upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	**E.** Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)*	**F.** TOTAL NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs	0	3	32	0	35
5. Cats	0	0	49	0	49
6. Guinea Pigs	0	0	109	0	109
7. Hamsters	0	0	13	0	13
8. Rabbits	0	136	176	0	312
9. Non-human Primates	1209	1087	1548	17	2652
10. Sheep	0	0	42	8	50
11. Pigs	0	0	221	0	221
12. Other Farm Animals	0	0	0	0	0
13. Other Animals					
VOLES	0	1338	274	0	1612
GERBILS	0	0	0	44	44

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)
I certify that the above is true, correct, and complete (7 U.S.C Section 2143)

SIG (b)(6)(b)(7)(c)

DATE SIGNED 11/30/2007

APHIS FORM 7023 (AUG 91) (Replaces VS FORM 18-23 (OCT 88), which is obsolete)

PART 1 - HEADQUARTERS

Exceptions to Regulations and Standards

Physical Restraint and Exemptions from Social Enrichment for Nonhuman Primates: Social Isolation

There are a variety of human diseases (Parkinson's Disease, Huntington's Disease, progressive supranuclear palsy, narcolepsy, and periodic leg movements during sleep) that are associated with uncontrolled movements in sleep that cause injury. Studies described here are on monkeys with Parkinsonism induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Monkeys given MPTP are kept in social isolation for periods of three days after drug administration while MPTP and its toxic metabolites are excreted. On a scheduled basis afterwards, these animals are placed in a cage specially designed for behavioral testing and telemetric recording in a room separated from the other monkeys. Individual monkeys may be maintained in the observation and recording room for a maximum of 14 days and are then returned to their home cage in a colony with other monkeys of the same species for at least 7 days before repetition. Isolation from other monkeys is necessary in order to permit sleep undisturbed by commotion caused by other monkeys or human traffic in and out of the room. Monkeys under study are instrumented with backpack transmitters which telemeter their EEG, EOG and EMG signals. This telemetric approach allows studying sleep behavior in monkeys that are unrestrained. In addition, physical restraint in a chair is done up to 8 times per month for 6-10 hours per session. This is done either to facilitate brain mapping, intracerebral recording, and neurochemical microdialysis or for fear-potential startle testing.

- Modulation of the sleep/wake state by dopamine (098-2005): 5 rhesus monkeys
- Cytokine-induced depression: A rhesus monkey model (223-2006): 12 rhesus monkeys.

Physical Restraint and Exemptions from Social Enrichment for Nonhuman Primates: Social Isolation

Capuchin monkeys under these conditions were used in studies (now discontinued) to determine how the brain is organized to control limb movement and how the brain reorganizes during the learning and acquisition of new skilled motor movements. Information gained from this research may improve the understanding of the neural basis of learning and may be applicable to better understanding of the brain response to stroke, trauma or other cerebral injuries. Physical restraint in a chair was done 3-5 times a week and lasted up to 1.5-4 hours per session in order to allow cortical stimulation testing and for conscious behavioral assessments. The animals were also housed singly, but otherwise in close proximity and within sight and sound of conspecifics. This must be done to prevent fight injuries to the hands and digits that would compromise motoneuron function or risk damage to subcutaneously implanted microelectrodes. Otherwise, full environmental and nutritional enrichments were provided.

- Muscle re-assembly in MI during skill acquisition (141-2005): 2 capuchin monkeys

Physical Restraint and Exemptions from Social Enrichment for Nonhuman Primates: Single-housing In Sight and Sound of Conspecifics:

Included in this section are primates that were housed in any condition other than group or pair housing for any significant period of time. For example, study subjects discussed below include those that were housed continuously in protected-contact housing, and those housed in protected-contact and/or group or pair housing for a significant portion, but not the entirety, of the period covered in this report.

A. Some animals used under these conditions are in studies of normal control of movement or motion disorders induced by MPTP. Monkeys given MPTP may be kept in social isolation for periods of three days after drug administration and while MPTP and its toxic metabolites are excreted. Before and after MPTP administration, monkeys in these studies are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. During these periods, monkeys with head appliances may also undergo short-term fixed head restraint to access the appliances for neurophysiologic recording and microdialysis. Additionally, the administration of the neurotoxin MPTP to induce Parkinson's Disease (PD) in macaques causes physical impairments that put such animals at risk of plummeting in the social order and wounding and fight injury from a cage mate. Consequently, animals given MPTP are generally housed singly, but in colony rooms within sight, sound and close physical proximity of other animals of the same species. Likewise, to prevent damage to expensive and sensitive surgically-implanted devices by a conspecific, monkeys may be housed singly, but otherwise within sight and sound of conspecifics.

- Analysis of the Neuronal Microcircuitry Basal Ganglia: 2 squirrel monkeys and 4 rhesus macaques
- Glutamate and GABA Related Therapies in Parkinson's Disease: 6 rhesus macaques
- Function of Dopamine in the Primate Substantia nigra; GABA-B Receptors and Parkinson's Disease: 6 rhesus macaques
- Influence of Subthalamic Nucleus of Striatal Dopamine: 4 rhesus macaques
- Regulation of Motor Function in Parkinson's Disease: Effects of CE in the MPTP Primate: 8 rhesus macaques

B. In the study of Alzheimer-like disease, animal will be studied following injections of lentiviral constructs in the brain following craniotomy. The safety and efficacy of immunizations also will be evaluated. Single or protected contact housing is required after surgery for 6 to 16 weeks to evaluate behavior or other clinical complications.

- Alzheimers Immunotherapy in Primate Model: 4 squirrels
- Focal Alzheimer APP Transgene Expression in Rhesus Monkeys: 4 rhesus

C. Infectious disease vaccine development studies may require single housing to prevent disease agent transmission. Some of the studies described here involve the development of a SIV/HIV vaccine, investigation of the role of host immune response in protecting against or contributing to the appearance of immune system damage following AIDS infection, evaluation of the function of the thymus during infection with SIV, evaluation of the development and pathogenicity of mutant viruses that develop over time in chronically infected animals, the effect of opiate dependency on the progression of AIDS, and the testing of the immunogenicity and efficacy of different AIDS vaccines and treatment regimens. Single housing is required after exposure to the virus to prevent transmission of virus from animal to animal. In addition, the animals need to be accessed frequently for blood draws. The experimental design requires that the efficacy of vaccines will be assessed after a single exposure and without the possible confound of exposure to mutant viruses. Infected animals

in an experimental group will be housed together after approximately one month. In some experiments, animals are singly housed one month prior to inoculation to allow sufficient time for acclimatization to the new housing arrangement so that the stress of separation doesn't influence susceptibility to or course of infection.

A study testing the effects of T cell depleting antibodies in SIV-infected mangabeys requires frequent antibody infusions and blood draws during the first 3 weeks of the treatment (animals are assessed up to 4 times per week), followed by weekly blood draws for the remainder of the study, which lasts 2 months. Because these animals will be frequently handled for testing, animals are housed in protected contact housing.

Malaria studies are being done to develop a vaccine and to provide antigens for serologic and molecular studies, genomic libraries, antibody production, and gametocytes for infection of mosquitoes. Chimpanzees infected with malaria are housed individually in metabolism cages. This is usually required for a period of 1-2 months. It is also necessary to house the animals indoors to prevent contact with the local mosquito population. Following blood collections and treatment of the malaria infection, the animals are returned to their normal housing environment. Protected-contact housing is utilized in other malaria vaccine studies in monkeys due to the requirement of daily heel or ear sticks (as well as blood collection and immunization), as well to avoid frequent reunions following stressful procedures. During the period to evaluate viral load and safety testing of gene therapy in a hepatitis C study, it is necessary to maintain the animals in metabolism cages. This is due to frequent blood collections and surgical interventions during the initial 4—6 weeks on study.

- Molecular Mechanisms of Antigenic Variations in Malaria: 19 rhesus macaques
- DN/MVA Immunogens, Cross-Clade Immune Response: 7 rhesus macaques
- GM-CSF as an Adjuvant for the Inactivated Polio Vaccine: 12 rhesus macaques
- Cellular Immune Responses and AIDS Pathogenesis: 13 rhesus macaques and 11 mangabeys
- Molecular Evolution of Multiply Deleted SIV in Vitro: 36 rhesus macaques
- Vaccination Against mucosal HIV Clade C Transmission: 27 rhesus macaques
- Mechanism of Oral SIV Transmission: 28 rhesus macaques
- Infant Immunoprophylaxis Against a Primate Lentivirus: 7 rhesus macaques
- SHIV Transmission Through Oral Versus Other Mucosae: 22 rhesus macaques
- Role of Virus Specific Immunity in Primate AIDS: 6 mangabeys and 21 rhesus macaques
- Molecular Analysis of Antigenic Variation in Malaria: 19 rhesus macaques
- Immune Modulation of Neurotropin in SIV Infection: 9 rhesus macaques
- Maintenance of Yerkes Primate Center Animal Colony: 176 rhesus macaques
- Project 3: Attenuated Listeria Vectors as an AIDS Vaccine in Macaques: 10 rhesus macaques
- Poxvirus Immunity and DNA/MVA HIV Vaccines: 32 rhesus macaques
- Therapeutic Vaccines for HIV: 17 rhesus macaques
- Determinants of Vaccine-Induced Memory T-Cell Development: 7 rhesus macaques
- Studies of the Natural Infectoin of Sooty Mangabeys: 20 sooty mangabeys
- Generation of /P. Vivax/ And DNA and Chromosones: 8 squirrel monkeys
- Genetics of Neuropathogenic SIV Infection: 9 pigtailed macaques
- Modulating HIV Immunity with Dendritic Cells: 25 rhesus macaques

D. Studies of dose and delivery vehicle in non-human primates have become a critical step to prepare for human clinical trials in lumbar fusion studies. Spine fusion surgery will be performed on animals followed by administration of different bone growth factors. Then animals will be in protected contact housing to prevent possible trauma to the surgical wound.

- Use of Osteoinductive Factors to Enhance Spine Fusion: 9 rhesus macaques

E. The integration of functional MRI (fMRI) technology with proven utility will significantly advance research efforts in biomedical and behavioral sciences. One proposal is directed towards brain activation studies during cocaine use. This may help to determine the brain structures and neural circuits that underlie the addictive properties of cocaine. In studies on cocaine and drug abuse, animals will be used for pharmacological and neurochemistry experiments involving the placement of an indwelling venous catheter for drug delivery during daily sessions lasting 1-2 hours. Some animals also have indwelling guide cannulae. The catheters and guide cannulae must be protected from contact by other animals. If contact is allowed, the preparations can be compromised with the risk of physical injury and infection. Protected contact housing reduces the risk since both animals can control proximity to others. The animals may require single housing if they persistently place themselves at risk to damage their indwelling venous catheters or guide cannulae, or that demonstrate a proclivity to damage another animal's catheter.

Determining the relationship between prefrontal cortical circuitry and components of dopaminergic neurotransmission is the focus of one research study that will enhance understanding of the cognitive processes subserved by the prefrontal cortex. This will hopefully shed light on human disease states, notably schizophrenia. In order to identify particular neural connections in the prefrontal cortex of macaques, axonal tracers will be injected intracerebrally. Following stereotaxic surgery, craniotomies will be made over the prefrontal cortex. Subjects must be in protected contact housing to protect craniotomy sites and sutures.

Assessment of specific roles of separate neuronal structures are performed on monkeys to evaluate the brain's response to damage at different ages. Studies will provide detailed descriptions of loss of memory functions, and other developmental disorders that occur. Single cage housing will be required for post surgical events until healing has occurred. Implants may require single cage housing to prevent damage to implants in incompatible animals.

- Transition States of Drug Addiction in Nonhuman Primates: 19 rhesus macaques
- PET Neuroimaging and Cocaine Neuropharmacology in Monkeys: 36 Rhesus macaques
- Cocaine use and Monoamine Function in Nonhuman Primates: 51 squirrel monkeys
- Analysis of the Neuronal Microcircuitry Basal Ganglia: 4 rhesus and 2 squirrel monkeys
- Orbitofrontal Limbic Ontogeny and Early Dysfunction: 18 rhesus macaques
- Development of Reversible Inactivation Technique: 2 rhesus macaques
- Imaging Medial Temporal Lobe Function: 2 rhesus macaques
- Brain Metabolic Effects of Deep Brain Stimulation: 2 rhesus macaques
-

F. Visual, vestibular and oculomotor systems must work together for normal visual function. Various disease processes or injuries can compromise the normal interaction of these systems. Research in this area will provide a basic science foundation for understanding eye movement control in humans. Primates are used since they exhibit the same set of eye movements as humans. To facilitate the research, sclera search-coils are implanted to precisely measure eye movement. In addition, head movements need to be restricted during visual testing to allow accurate tracking of visual targets. Therefore, a stainless-steel receptacle is implanted. It is sometimes necessary to house animals in protected housing when they have surgical implants. This is to protect the animal from any injury due to aggressive behavior of other animals. Animals also sometimes wear goggles which may be removed during paired housing.

- Neural Control of Visual Vestibular Behavior: 6 rhesus macaques
- Visual Processing and Smooth Eye Movement: 22 rhesus macaques
- Binocular Coordination of Eye Movements in Monkeys: 10 rhesus macaques

I. Studies of pancreas, kidney, and bone marrow transplants as well as arterial grafts are investigating the ability of costimulation blockade to protect the organs from rejection. For experiments involving bone marrow transplantation, single housing is required for the first 75-100 days following the transplant due to the potential complications including immunosuppression, anemia, leukopenia and thrombocytopenia. After that time, the animals may be paired with same sex and age animals. In the pancreatic islet cell transplant model, daily monitoring of urine and stool output are necessary to diagnose steatorrhea, polyuria and ketoacidosis. In addition, pancreatic enzyme replacement and Rapamycin are administered orally in a treat and it is essential that the amount consumed by each animal is recorded. Following renal transplantation, animals will require protected housing so that an accurate assessment of daily food/water intake and urine/feces production be accounted. Prior to surgery, animals may be pair-housed. With immunosuppressive therapy, healing can be delayed. A study using nonhuman (mouse) stem cells involves inoculation of the cells in the nonhuman primate model to evaluate survival of the cells and effects on the recipients.

- Costimulation, Chimerism and Tolerance in Transplantation: 64 rhesus macaques
- Injection of Immune Privileged Mouse Progenitor: 2 rhesus macaques

<u>Physical Restraint, Exemptions from Social Housing, and Food or Water Restriction of Nonhuman Primates</u>

Nonhuman primates used under these conditions are in motion disorder studies or studies of brain function. Most of the animals are used to research the cause and treatment of Parkinson's Disease (PD) because of the great similarity of brain function and that Parkinson's-like disease can be induced in them by giving the neurotoxic chemical – MPTP. Monkeys in these studies usually are given MPTP by intracarotid injection, so that only one side of the brain is affected. These monkeys have only slight deficits in precise control of movements on one side of the body and have no substantial movement problems. In general, isolation housing is only done for a 3 day period immediately after administration of MPTP during the time of excretion of the neurotoxin in the feces and urine. Otherwise, monkeys in these studies are housed within sight and sound of other animals of the species and permitting physical contact with a compatible conspecific.

Monkeys in studies requiring food or water restriction are provided *ad libitum* food and water on weekends according to standard husbandry practices. During weekdays, food or water is restricted overnight and in the morning (12-15 hours total) and then food or water is provided to

satiety during morning or afternoon test sessions as an inducement to perform video-based tasks. Single housing is necessary to facilitate food or water restriction – otherwise a conspecific would be subjected to unnecessary restriction or food sharing might occur. Monkeys are trained using food or water as an inducement to perform simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. These monkeys, except as indicated, are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. During these periods, the monkeys with head appliances may also undergo short-term fixed head restraint to access the appliances for neurophysiologic recording and microdialysis. Water or food is provided during and immediately after the testing session to meet the daily ration. The total intake of the restricted material, food or water, is recorded daily and the animal's body weight is checked and recorded at least twice weekly to ensure that are being well maintained.

In eye movement studies, animals must be awake, alert and comfortably seated. The tasks involve following a smoothly moving or jumping target spot that is rear-projected on a tangent screen. First the animals are fitted with a collar that it will always wear. It is made of a soft nylon material. Animals are then adapted to pole handling and using a primate chair. It takes most animals 4 weeks to reach proficiency. Animals are trained 5 days per week for time periods of 15 minutes to 3 hours.

A study to develop a transgenic model of Huntington's Disease uses the primate chair during semen collections and, again, during cognitive testing procedures for offspring produced. In these tests, the monkeys are habituated to the use of a chair over a one to two week period before performing the task for preferential looking while sitting with free movement of arms and legs.

In cocaine abuse studies, cocaine is scheduled as the consequent event and is sufficiently reinforcing that food and water restrictions are not necessary. However, for self-administration experiments, subjects are trained to sit quietly in standard primate chairs over a 2-4 week period. The pole-and-collar system for handling and training nonhuman primates will facilitate immobilization. Initially, subjects will be immobilized for approximately 20-30 minutes per training session, but over the course of several weeks, the amount of time will increase to from 1 to 4 hours per session. Each subject will be immobilized at least twice per week for 6 weeks. In a related study, changes in sensitivity to the CNS effects of cocaine are assessed after the monoamine neurotransmitter is manipulated pharmacologically. The animals are trained to be seated in a loosely fitting chair during daily (Mon. – Fri.) sessions. The chair is designed to provide minimal skin contact with the animal, and is limited primarily to the waist and buttocks. Typically, experiments are conducted so as to require no more than one hour per day in the apparatus. This minimal restraint provides protection of indwelling catheters used for drug administration and contact with a localized area of the tail for electrical stimulation.

Startle reflex testing is done in one study after each monkey is habituated to chair restraint. The sessions are 2-3 times per week for 60 minutes each session. The tests continue for 2 weeks. These tests may be repeated every 3-4 months to monitor potential developmental changes in emotionality.

Some of the animals used under these conditions are in oculomotor, visual disorders, and visual cortex studies. Monkeys are used because they are capable of the same range of eye movements as humans. Infant monkeys are swaddled in a blanket. Older animals have a chair adjusted for comfort. The chair includes a standard design that allows the animal to sit in a natural position. The animal is allowed to sit in the chair for 5-15 minutes on the first occasion, during which time

treats (apple slices, applesauce, etc) are offered to make the chair session a positive experience. Head movements in the animals during visual testing are restricted by an implanted stainless steel receptacle (SSR) on the head. In other studies, head movement is restricted with a custom-fit helmet.

In these studies with transiently-induced movement disorders or studies of midbrain function, monkeys are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. Animals assigned to studies to distinguish different types of cognition or memory may be tested in homecages, specifically designed rooms or using physical restraint.

To motivate the animals to work effectively, the first feeding of the day may be reduced or delayed. However, water or food is provided during and immediately after the testing session to meet the daily ration. The total intake of the restricted material, food or water, is recorded daily and the animal's body weight is checked and recorded at least twice weekly to ensure that are being well maintained.

1. Food and/or water restricted, but provided during and after laboratory testing sessions:

- Subcontract "Effects of Viewing Distance on Eye Growth and Refractive Development: 4 rhesus macaques
- Binocular Coordination of Eye Movements: 10 rhesus macaques
- Episodic Memory in Rhesus Monkeys: Spatial and Temporal Contexts: 6 rhesus macaques
- Cellular Mechanisms Underlying the Therapeutic Benefit of High-Frequency Stimulation of the Subthalamic Nucleus for Parkison's Disease: 2 rhesus macaques
- Local Field Potentials in the Basal Ganglia: 4 rhesus macaques
- Neural Control of Visual Vestibular Behavior: 6 rhesus macaques
- Neurology of Memory in the Nonhuman Primate: 15 cynomolgus macaques

2. Short-term physical restraint only:

- Binocular Coordination of Eye Movements: 10 rhesus macaques
- Sugars as Novel Cyoprotectants for Primate Oocytes: 5 rhesus macaques
- Function of Dopamine in the Primate Substantia Nigra: GABA-B Receptors and Parkinson's Disease: 6 rhesus macaques
- Maintenance of Yerkes Primate Center Animal Colony: 172 rhesus macaques
- Transition States of Drug Addiction in Nonhuman Primates: 17 rhesus macaques
- Regulation of Motor Function in Parkinson's Disease: 9 rhesus macaques
- Behavioral, Neural and Endocrine Covariates of Differential Rearing History in Juvenile Macaca Mulatta: 59 rhesus macaques
- Behavioral Effects of Neonatal Amygdala Lesions in Monkeys Living in the Semi-Naturalistic Environment: 4 rhesus macaques
- Development of a Reversible Deactivation, via Cooling Technique to Study Higher Cognitive Function in Monkeys: 2 rhesus macaques
- PET Neuroimaging and Cocaine Neuropharmacology in Monkeys: 36 rhesus macaques
- Orbitofrontal Limbic Ontogeny and Early Dysfunction: 18 rhesus macaques

- Development of Reversible Inactivation Technique for the Study of Higher Cognitive Functions in Monkeys: 2 rhesus macaques
- Development of Medial Temporal Lobe Function: 22 rhesus macaques
- Basal Ganglia Discharge Patterns in Parkinsonism: 5 rhesus macaques
- Laminar Specific Neural Mechanisms for Memory in the Entorhinal Cortex: 2 rhesus macaques
- Neural Control of Visual Vestibular Behavior: 6 rhesus macaques
- Relationship between Nearwork and the Development of Myopia: 2 rhesus macaques
- Visual Processing & Smooth Eye Movements: 22 rhesus macaques
- Transgenic Monkey Inherited Neurodegenerative Disease: 48 rhesus macaques
- Neurology of Memory in the Nonhuman Primate: 15 cynomolgus macaques
- Cocaine Use and Monoamine Function in Nonhuman Primates: 36 squirrel monkeys

Exemptions from Exercise for Dogs

Dogs with an inherited motoneuron disease may be restricted from exercise for 3-4 days while acutely recovering from surgery although it should be noted that no surgery or research procedures were done during this reporting period.

- Title: Functional studies in motoneuron disease (149-2006): 7 dogs.

Physical Restraint of Sheep

Sheep are used in studies of the effect of gene therapy or pharmacologic agents (including inhaled) upon the pulmonary epithelium and general physiology. These studies are intended to better understand the pathophysiology and improvement treatment of conditions such as pulmonary hypertension, acute lung injury, and ARDS. In the conduct of the research procedures, sheep are loosely restrained in small ruminant stanchions for up to five hours to enable hemodynamic and pulmonary physiology measurements while under continuous observation.

- Title: C/EBPbeta regulation of lung inflammation (080-2004): 26 sheep

Summary of Studies (Animal) Listed in Column E

Title: Modulation of the sleep/wake state by dopamine (098-2005)

- 5 Rhesus Macaques

Disorders affecting dopamine transmission, such as Parkinson's Disease, are associated with disrupted sleep patterns and arousal. Rhesus monkeys are used in this study to investigate the cellular mechanism of these sleep disorders and how medications act and can be better used to manage them. Nonhuman primates given the neurotoxin MPTP are used as a model of parkinsonianism. Induction of parkinsoniansim with MPTP causes impaired movement, blunted motivation, apathy and drowsiness that may be distressful. This condition cannot be relieved with pain-relieving drugs. In fact, analgesics, anesthetics and tranquilizers are medically contraindicated for the condition potentially enhancing drowsiness and creating risk of aspiration or respiratory distress. Although the federal reporting requirements only considers the use of anesthetics, analgesics and tranquilizers to relieve pain or distress, it should be noted that

dopaminomimetic agents, a more specific and appropriate intervention, may be used to reverse acute signs of MPTP intoxication in animals on this study. The five animals reported with this work were carried-over from 2006 and do not represent new acquisitions.

Title: Cytokine-Induced Depression: A Rhesus Monkey Model (223-2005)

- 12 Rhesus Macaques

Human patients with a wide range of illnesses may exhibit a high rate of depression mediated by activation of the immune system and the release of cytokines. The latter can exert effects upon the brain leading to altered behavior. For example, about 50% of humans given the cytokine IFN-alpha therapeutically develop depression. In these studies, the administration of IFN-alpha causes chronic immune activation and a behavioral syndrome in macaques similar to depression in humans. Monkeys given the cytokine are used to study how it disrupts brain neurochemistry and to develop treatment interventions. The syndrome may also be characterized by apathy, poor motivation and sleepiness. Potentially animals may also experience heightened sensitivity to painful stimuli and other neurological abnormalities. Pain relieving drugs, except during and immediately following surgery, cannot be used because of the potential confounding effects upon the neurological effects of the model as well as increasing the risk of sleepiness, respiratory depression and aspiration. The 12 animals reported with this study were carried-over from the 2006 census and do not represent new acquisitions.

Title: C/EBPbeta regulation of lung inflammation (080-2004)

- 8 sheep

Inflammatory diseases of the lung cause respiratory dysfunction, may involve infectious agents and often with a septic component, and may cause high mortality. To simulate sepsis and associated pulmonary pathology in a controlled and self-limiting fashion, sheep are administered endotoxin by intravenous injection. The host response to the endotoxin elicits a cascade of events resulting in hypoxemia, pulmonary hypertension, pulmonary inflammation and edema, and respiratory distress lasting for several hours. Additionally, sheep experience transient fever, malaise and other flu-like symptoms lasting 12-15 hours before restoration to normal health. The administration of pain relieving agents, both narcotics and nonsteroidal anti-inflammatory drugs, may alter inflammatory effect, immune response and, if tranquilizing, respiratory function. Such would confound the interpretation of scientific data making the use of anesthetics, analgesics or tranquilizers contraindicated in the model. All 8 of these sheep were new acquisitions.

Title: Anatomy and Pharmacology of Fear Potential Startle (019-2005)

- 44 Gerbils

The understanding of neural systems involved in conditioned fear using the fear startle test as a measure has been identified as relevant to identifying critical events in the formation of fear and anxiety in human anxiety disorders. The study may cause discomfort or pain that cannot be treated with general anesthetics without compromising expected results. The gerbil, the rodent species with the NK1 receptor similar to the human, is given footshocks to evaluate the effects of prior classical conditioning on startle amplitude used as the measure of anxiety.